



DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

JAN 7 1974

Request for Proposal No. NCI-CB-43939-37
Title: Biochemical and Physiological Investigations Based on Familial
Genetic Patterns.

Gentlemen:

The National Cancer Institute is soliciting proposals for the above titled research project. Your organization is among the sources invited to submit a proposal for this work. It is our policy in the solicitation and negotiation of research contracts to secure the best qualified organization available to perform the work, cost and other factors considered. We intend to screen all proposals received in the most objective manner possible, employing the technical evaluation criteria listed in Part II of this Request for Proposal.

Please carefully review all parts of this Request for Proposal (RFP) before preparing and submitting a contract proposal.

Thirty copies of your proposal should be submitted to Contracting Officer, National Cancer Institute, Research Contracts Branch, OD, NCI, Landow Building, Room C-437, Bethesda, Maryland 20014 and must be received no later than the close of business, 5:00 p.m., local time, on February 5, 1974. Your outside envelope should be marked "NOT TO BE OPENED BY THE MAIL ROOM."

If you have any questions concerning the requirements of this solicitation, address them to Mr. Phillip J. Webb, Contracting Officer, NCI, telephone: Area Code 301-496-5565 (collect calls will not be accepted). Any questions pertaining to the technical scope of work must be submitted in writing.

Sincerely yours,

P. J. Webb
Contracting Officer, DCBD
Research Contracts Branch
National Cancer Institute

Enclosure

I. WORKSCOPE

Objective for Study I

The availability of well delineated high and low risk breast cancer family kindreds offers an important opportunity to evaluate the possible role of genetic factors in the expression of specific biochemical parameters in breast cancer pathophysiology. In view of the long appreciated importance of endocrine factors in breast cancer and the notable absence of familial studies in this area, the following study may clarify much of the confusion in the field of breast cancer regarding such hormonal factors as the urinary estriol quotient, the role of lactogenic hormones, corticoid-androgens discriminants, etc. in the pathogenesis of breast cancer.

Workscope for Study I

Independently and not as an agent of the government the contractor shall carry out biochemical investigations on female members of families with a high and low risk of breast cancer. These studies shall include the following:

1. Endocrine assays on blood and urine of premenopausal females from families with a high incidence of breast cancer and from matched control families. Matching should be done for age, race, fertility history, birth control medication, etc. The analysis to be performed should include:

- (a) basal body temperature charts for three months
- (b) daily 12 hour nocturnal urine collections for one complete cycle
- (c) one 24 hour follicular and one 24 luteal urine in the cycle
- (d) alternate daily 15-20 ml blood samples on all for one cycle
- (e) blood assays: FSH, LH, E₃, E₂, E₁, progesterone and prolactin
- (f) urine assays: 11-13 estrogenic, androgenic and corticosteroid metabolites.

2. This study is expected to last two years but may be extended for quality control and additional subjects.

Objective for Study II

Recent studies by Gelboin indicate that aryl hydrocarbon hydroxylase (AHH) enzymes may be important in the mechanism of hydrocarbon carcinogenesis. Recently, Shaw and associates reported the presence of a genetic variation in the activity of aryl benzpyrene hydroxylase (BP-hydroxylase) in leucocytes. These investigators consider it possible that this enzyme assay may prove a means to predict risk of future lung cancer. It is felt important that measurements of the physiological markers such as the enzyme, aryl hydrocarbon hydroxylase (AHH) and possibly others, should be studied from well delineated family kindreds of high and low risk for breast cancer.

Workscope for Study II

1. Aryl hydrocarbon hydroxylase (AHH) studies or studies of other physiological markers should be done on female members of high and low risk breast cancer families.
2. About 20 multiple case families should be studied as well as matched controls.
3. Study II may be done in conjunction with the endocrine studies outlined above in Workscope Study I or may be done separately.
4. These studies may be done by separate investigators or a collaborative group using its own patient resource or the patient resource of the Breast Cancer Task Force.